

Wide resection of soft tissue sarcomas after unplanned primary procedures

A long-term follow-up study

Jian Kang, MD, PhD, Ming Xu, MD, PhD, Bing Wang, MD, PhD, Xiuchun Yu, MD, PhD*

Abstract

Unplanned resection of soft-tissue sarcomas (STS) predispose the patients to recurrences and metastases, secondary wide resection is usually warranted.

To investigate the outcomes of re-excision of STS after unplanned initial resection.

The records of 39 patients undergoing re-excision of STS after unplanned initial resection from January 2006 through December 2015 were retrospectively investigated.

There were 17 males and 22 females, the mean age was 45.7 years. Most initial unplanned resections were performed in rural hospitals by surgeons from general surgery department, dermatology department, plastic surgery department, and orthopedic department. Thirty-five patients underwent secondary wide resections in our department. Histopathological findings indicated positive margins after primary surgeries in 18 patients. Until the conclusion of 37.2-month follow-up, 7 patients developed metastasis, 3 had local recurrence, and 7 were dead. Positive margins were associated with increased metastases and lower survival rates ($P < .05$). There was no significant difference in recurrences between the 2 groups.

Unplanned initial resection of STS often lead to unfavorable prognosis. Primary wide resections are warranted for this disease entity.

Abbreviations: CT = computed tomography, STS = soft-tissue sarcoma.

Keywords: re-excision, soft tissue sarcoma, survival rate, unplanned initial excision

1. Introduction

Soft-tissue sarcomas (STSs) are primary malignant tumors constituting less than 1% of all malignancies with an incidence of 1 to 2/100000.^[1-3] Whereas benign soft-tissue tumors are more common with an incidence of 300 times as STS.^[4] Due to

the rarity of STS, superficial masses are usually resected as benign tumors, and pathological examinations are often ignored. Most of these operations are performed by surgeons without specialty training in oncology,^[5,6] such as general surgeons, plastic surgeons, orthopaedic surgeons and dermatologists from rural hospitals. Despite the ever increasing training program regarding treatment of STS, unplanned resections are still common in China, especially in underdeveloped area.

Editor: Leonidas G. Koniaris.

JK is considered as first author, as well as XY is considered as corresponding author of this submission.

This study was approved by the Medical Ethics Committee of the 960th hospital of People's Liberation Army. Written informed consent was obtain from the patients or patients' family for publication of this study and accompanying images.

The authors have no conflicts of interest to disclose.

Department of Orthopaedics, The 960th hospital of People's Liberation Army, 25 Shifan Road, Jinan, Shandong Province, China.

* Correspondence: Xiuchun Yu, Department of Orthopaedics, The 960th hospital of People's Liberation Army, 25 Shifan Road, Jinan, Shandong Province, 250031, China (e-mail: startdmxx@foxmail.com).

Copyright © 2020 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Kang J, Xu M, Wang B, Yu X. Wide resection of soft tissue sarcomas after unplanned primary procedures: A long-term follow-up study. *Medicine* 2020;99:8(e19067).

Received: 26 July 2019 / Received in final form: 7 December 2019 / Accepted: 7 January 2020

<http://dx.doi.org/10.1097/MD.00000000000019067>

2. Materials and methods

2.1. Patients

From January 2006 through December 2015, 39 patients with STS who had received unplanned resections were referred to our institution for further treatment. There were 17 male patients and 22 female, the mean age was 45.7 years (range, 18 to 78 years). The tumor locations included the trunk in 12 cases (30.7%), upper extremities in 9 (23.1%), and lower extremities in 18 (46.2%). Histological diagnoses included synovial sarcoma, dermatofibrosarcoma protuberans and undifferentiated pleomorphic sarcoma. More than 85% patients had undergone initial unplanned resections of tumors in village clinics, municipal- and county-level hospitals. Furthermore, most of the unplanned procedures were performed by general surgeons, plastic surgeons, orthopaedic surgeons, and dermatologists. Positive margins were determined by histopathological findings in 18 patients. No patients had received neoadjuvant chemotherapy before the primary surgery. (Tables 1 and 2)

Table 1**Sex and site distribution about different histological types of STS in our patients.**

Histological type of STS	No. of patients	Gender		Site		
		Male	Female	Thunk	upper extremity	Lower extremity
synovial sarcoma	10	5	5	0	1	9
Malignant fibrous histiocytoma	8	4	4	7	1	0
Dermatofibrosarcoma protuberans	8	2	6	3	2	3
Liposarcoma	5	2	3	1	1	3
Leiomyosarcoma	2	1	1	0	1	1
Alveolar rhabdomyosarcoma	1	1	0	0	1	0
Pleomorphic rhabdomyosarcoma	1	0	1	0	0	1
Myxofibrosarcoma	1	1	0	0	1	0
Clear cell sarcoma	1	1	0	1	0	0
Epithelioid fibrosarcoma	1	0	1	0	0	1
Primitive neuroectodermal tumors	1	0	1	0	1	0

2.2. Treatment Strategy

Treatment algorithm for patients undergoing unplanned resection of STS was as follows: 35 patients received secondary wide resection of tumor. Intraoperative frozen sections indicated negative margins were achieved. Postoperative chemotherapy was applied in 14 patients. Two patients received amputation for unresectable STS. One patient with multiple metastases received chemotherapy without having surgeries. One patient received chemotherapy based on positron emission tomography-computed tomography (CT) and pathological findings.

2.3. Evaluation

The endpoints of the follow-up were deaths. Follow-up was carried out through telephone and out-patient clinic interview. Recurrences were detected with use of ultrasonic examinations and magnetic resonance imaging. Rates of local recurrence, metastasis and 5-year survival were compared between patients with and without positive margins after primary surgery.

2.4. Statistical Analyses

All statistical analysis was performed by using SPSS software (version 13.0, IBM, Armonk, NY), with statistical significance being set at $P < .05$.

3. Results

According to the pathologic findings in secondary procedures, 18 patients had positive margins after primary surgeries. Fortunately, negative margins were achieved in all 35 patients after secondary wide resection. One patient had infection after primary procedures, and had vacuum scaling drainage followed by

secondary wound closure with use of local flap. No patients had motor/sensory dysfunction. All cases were followed up for at least 10 months (from 10 to 127 months, mean 37.2 months). 7 patients had metastases, 3 had recurrences, and 7 were dead. The 5-year overall survival rate was 80.5% (Table 3, Fig. 1).

3.1. Local recurrence

Two in 18 patients with positive margins had local recurrences, whereas 1 in 21 having negative margins had recurrences. There was no significant difference in recurrence between the 2 groups ($P = .441$; Table 4)

3.2. Metastasis

Six patients presenting with positive margins had metastases. The metastasis rate in patients with positive margins was significantly higher than that of patients with negative margins (1 of 21 patients; $P = .027$; Table 4)

3.3. Rate of survival

The 5-year survival rates were 64.5% and 95.2% in patients with and without positive margins respectively. There was significant difference between the 2 groups. ($P = .028$; Table 4, Fig. 2)

Table 3**Characteristics of 39 patients with unplanned initial excisions.**

Index	Values
Age, yr: range, mean	18–78, 45.7
Gender	
Male	17
Female	22
Residual diseases	
Positive	18
Negative	21
Re-resections	
Yes	35
No	4
Chemotherapy after re-resections	
Yes	14
No	25
Follow-up time, mo: range, mean	10–127, 37.2
Total 5-yr survival rates	80.5%

Table 2**The level of hospitals where unplanned initial excisions were performed.**

Level of hospitals	No. of patients	Without residual tumor	With residual tumor
Provincial-level	5	4	1
municipal-level	10	6	4
county-level	21	10	11
village clinics	3	1	2

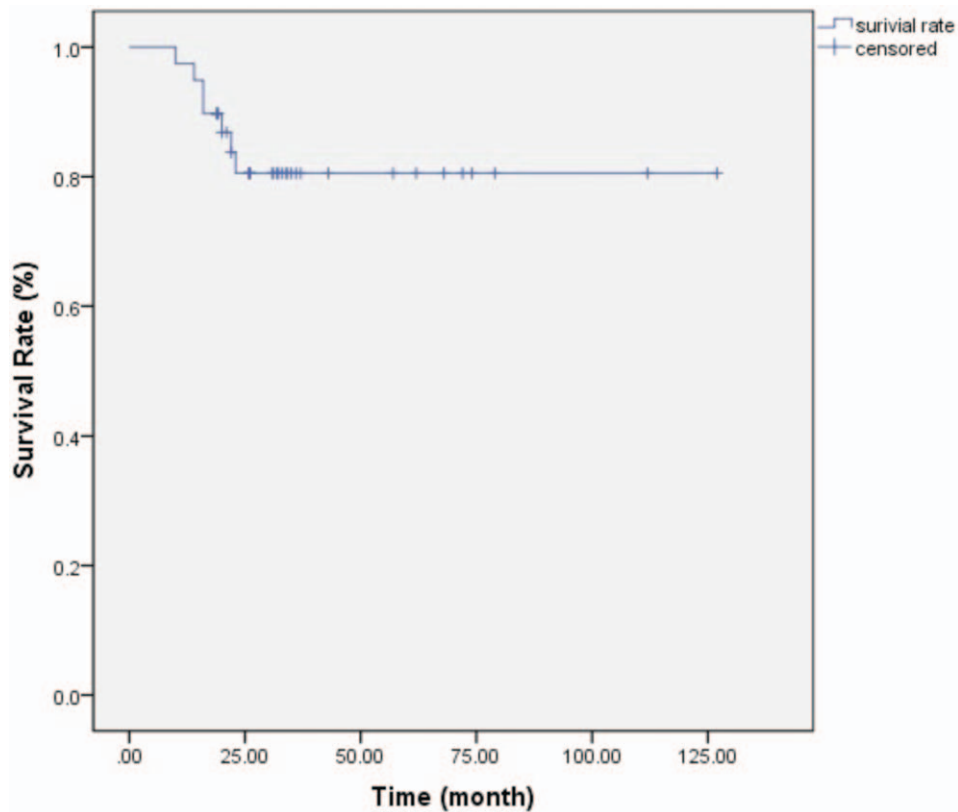


Figure 1. Overall 5-year survival rate of 39 patients.

4. Discussion

In clinical practice, patients with STS often have improperly designed procedures due to misdiagnosis. In the present study, of the 39 STS patients undergoing unplanned initial procedures, only 5 patients were operated on in provincial-level hospitals, no procedures were performed by specialized oncological surgeon. Some of the primary procedures were carried out by general surgeons, plastic surgeons, orthopaedic surgeons, and dermatologists. No cases had biopsy and intraoperative frozen section. According to pathological findings, 16 patients had positive margins after primary procedures. Studies investigating the outcome of unplanned primary surgeries for STS are sparse. Kang et al suggested the recurrence rate was significantly lower in patients

referred to tertiary hospitals than in those from other medical institutes.^[7] In this study, we did not compare the outcomes of treatment among hospitals of different levels because only 5 patients underwent unplanned primary procedures in provincial-level hospital. However, we found the rates of positive margin was higher in lower-level hospitals than in provincial-level hospital.

Thirty-five patients received secondary wide resections in our department. However, the procedures were associated with some drawbacks, such as extensive tissue removal, prolonged operation time, functional loss and increased risk of local recurrence.^[8] Of the 35 patients, it is difficult to determine the surgical safety margin before the re-resection due to the interference of the post-operative reactive changes on CT or magnetic resonance imaging.^[9,10] Therefore, we had to perform more extensive resection than standard procedures. Furthermore, intraoperative frozen section was mandatory. Skin grafting was used in 1 patient due to significant tissue defect. Therefore, the length of hospital stay was prolonged and the medical expenses raised.

Some authors suggested unplanned resection is not an independent risk factor for unfavorable oncological outcome in terms of local recurrences, metastases, and overall survival.^[4,11] However, disputes remains about this clinical issue.^[12,13] The inconsistency of previous findings in the literature might be related to failure of including positive margins as a risk factor for the prognosis. Sixteen patients did not obtain negative margins according to the pathological findings after primary procedures and 2 patients had positive margins in the first resection according to the second wide resection in our department. Similarly, previous studies reported a positive margin rate of 35%

	With residual tumor	Without residual tumor	P value
Local recurrence			.441
Yes	2 (11.1%)	1 (4.8%)	
No	16 (88.9%)	20 (95.2%)	
Time, mo	10.50 ± 0.50	8	
Metastasis			.027
Yes	6 (33.3%)	1 (4.8%)	
No	12 (66.7%)	20 (95.2%)	
Time, mo	8.50 ± 2.87	8	
5-yr Survival rate	64.5%	95.2%	.028

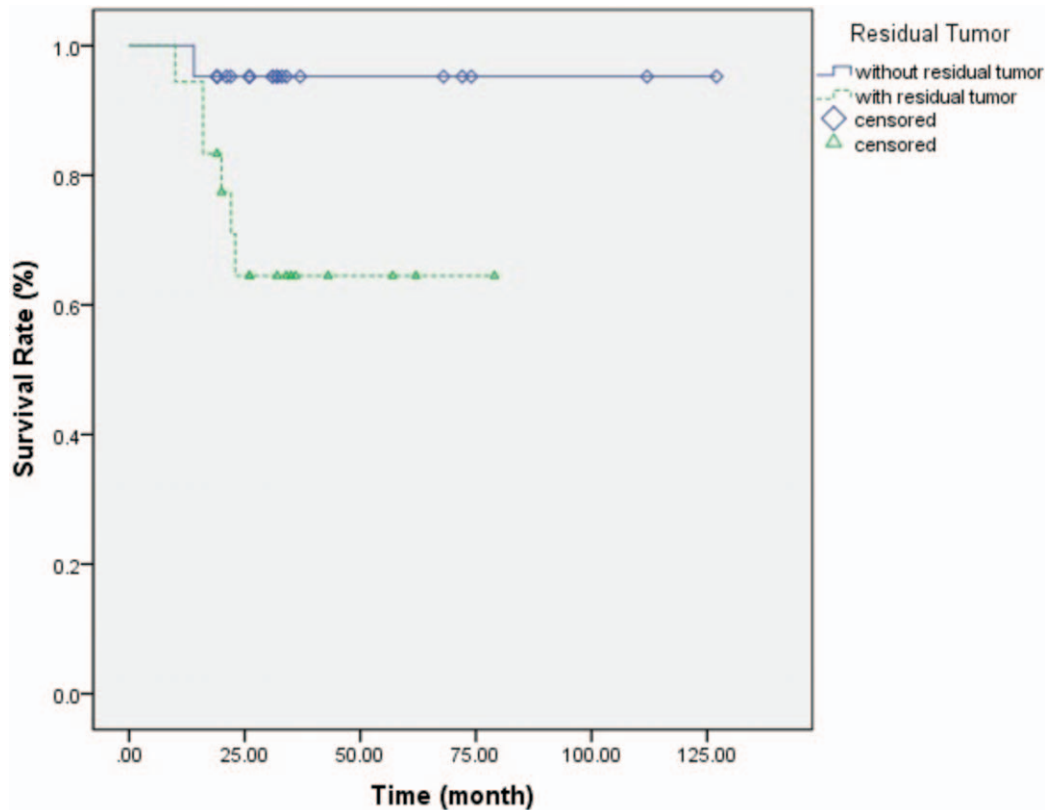


Figure 2. Comparison about 5-year survival rate between patients with and without residual tumor.

to 56% after unplanned resections.^[14–16] As for local recurrences, our findings demonstrated residual tumor after unplanned resections was not an independent risk factor for patients undergoing unplanned primary procedures. However, the rate of metastases in patients with positive margins after initial primary procedures was significantly higher and the overall survival rates was lower than that of patients with negative margins. Our findings are contrary to that of previous literature.^[17–19] We deduce such inconsistent results might be attribute to different time and resection magnitudes. Extensive resection and intraoperative frozen section might explain the low rate of local recurrence in this study. Otherwise, unplanned primary resection with positive margins destroyed the capsule of the tumor, and longer interval between unplanned resection and re-resection might increase the possibility of metastasis. On the other hand, secondary procedures for the cases of positive margins may activate tumorigenic mechanisms, this could exert negative impacts on survival.^[20]

Adjuvant radiotherapy or chemotherapy are necessary for STS, especially for patients with positive margins after unplanned primary procedures. Kepka et al^[21] reported adjuvant radiotherapy was an effective treatment for patients undergoing re-resection, the 10-year local and distant control rates were 86% and 80% respectively. Adjuvant chemotherapy is used for certain types of chemo-sensitive sarcomas, but the literature showed no significant effects on distant metastases and survival.^[22] Furthermore, neoadjuvant chemotherapy is usually used in locally advanced sarcomas to decrease the recurrence and metastasis rates of initial excision with negative

surgical margins. In this study, due to the heterogeneity of pathological diagnoses, it would be of no clinical significance to investigate the relationship between survival and chemotherapy.

5. Conclusions

Unplanned primary resection of STS is common.^[6,20,23,24] Wide resection is mandatory for favorable outcomes. Furthermore, patients with positive and uncertain margins after primary surgery should have secondary resection as soon as possible. Extensive resection and intraoperative pathological determination are important to improve the outcome of secondary procedures. If the demerits of unplanned resection and the knowledge of soft tissue tumor had been well recognized by the surgeon of lower level hospitals, unplanned resection of soft tissue tumor would be less and more patients with soft tissue tumor would receive professional treatment. For this purpose, our department have organized about 20 lectures about bone and soft tissue sarcoma in different cities of Shandong Province of China in the past 3 years. We believe that the diagnosis and treatment of soft tissue sarcoma in Shandong Province would be improved in the near future.

Acknowledgments

We sincerely thank the contribution of all patients to the publication of this study.

Author contributions

Data curation: Jian Kang, Ming Xu, Bing Wang.

Project administration: Xiuchun Yu.

Writing – original draft: Jian Kang.

Writing – review and editing: Xiuchun Yu.

References

- [1] Westbury G. The management of soft tissue sarcomas. *J Bone Joint Surg Br* 1989;71:2–3.
- [2] Boring CC, Squires TS. Cancer statistics, 1993. *CA Cancer J Clin* 1993;43:7–26.
- [3] Greenlee RT, Hill-Harmon MB, Murray T, et al. Cancer statistics, 2001. *CA Cancer J Clin* 2001;51:15–36.
- [4] Fiore M, Casali PG, Miceli R, et al. Prognostic effect of reexcision in adult soft tissue sarcoma of the extremity. *Ann Surg Oncol* 2006;13:110–7.
- [5] Siegel HJ, Brown O, Lopez-Ben R, et al. Unplanned surgical excision of extremity soft tissue sarcomas: patient profile and referral patterns. *J Surg Orthop Adv* 2009;18:93–8.
- [6] Venkatesan M, Richards CJ, McCulloch TA, et al. Inadvertent surgical resection of soft tissue sarcomas. *Eur J Surg Oncol* 2012;38:346–51.
- [7] Seungcheol Kang, Ilkyu Han, Sang A, et al. Unplanned excision of soft tissue sarcoma: the impact of the referring hospital. *Surgical Oncology* 2013;17–22.
- [8] Potter BK, Adams SC, Pitcher JD, et al. Local recurrence of disease after unplanned excisions of high-grade soft tissue sarcomas. *Clin Orthop Relat Res* 2008;466:3093–100.
- [9] Kaste SC, Hill A, Conley L, et al. Magnetic resonance imaging after incomplete resection of soft tissue sarcoma. *Clin Orthop Relat Res* 2002;397:204–11.
- [10] Sugiura H, Takahashi M, Katagiri H, et al. Additional wide resection of malignant soft tissue tumours. *Clin Orthop Relat Res* 2002;394:201–10.
- [11] Arai E, Nishida Y, Tsukushi S, et al. Clinical and treatment outcomes of planned and unplanned excisions of soft tissue sarcomas. *Clin Orthop Relat Res* 2010;468:3028–34.
- [12] Umer HM, Umer M, Qadir I, et al. Impact of unplanned excision on prognosis of patients with extremity soft tissue sarcoma. *Sarcoma* 2013;2013:498604.
- [13] Potter BK, Adams SC, Pitcher JD Jr, et al. Local recurrence of disease after unplanned excisions of high-grade soft tissue sarcomas. *Clin Orthop Relat Res* 2008;466:3093–100.
- [14] Noria S, Davis A, Kandel R, et al. Residual disease following unplanned excision of soft-tissue sarcoma of an extremity. *J Bone Joint Surg* 1996;78:650–5.
- [15] Goodlad JR, Fletcher CDM, Smith MA. Surgical resection of primary soft-tissue sarcoma. Incidence of residual tumour in 95 patients needing re-excision after local resection. *J Bone Joint Surg* 1996;78:658–61.
- [16] Serpell JW, Ball ABS, Robinson MH, et al. Factors influencing local recurrence and survival in patients with soft tissue sarcoma of the upper limb. *Br J Surg* 1991;78:1368–72.
- [17] Lewis JJ, Leung D, Espat J, et al. Effect of re-resection in extremity soft tissue sarcoma. *Ann Surg* 2000;231:655–63.
- [18] Zagars GK, Ballo MT, Pisters PWT, et al. Surgical margins and re-resection in the management of patients with soft tissue sarcoma using conservative surgery and radiation therapy. *Cancer* 2003;97:2544–53.
- [19] Davis AM, Kandel RA, Wunder JS, et al. The impact of residual disease on local recurrence in patients treated by initial unplanned resection for soft tissue sarcoma of the extremity. *J Surg Oncol* 1997;66:81–7.
- [20] Atalay C, Cetin B, Zarali O. The impact of re-excision on survival after unplanned resection in extremity soft tissue sarcomas. *Asia Pacific J Clin Oncol* 2005;1:71–6.
- [21] Kepka L, Suit HD, Goldberg SI, et al. Results of radiation therapy performed after unplanned surgery (without re-excision) for soft tissue sarcomas. *J Surg Oncol* 2005;92:39–45.
- [22] Karakousis CP, Driscoll DL. Treatment and local control of primary extremity soft tissue sarcomas. *J Surg Oncol* 1999;71:155–61.
- [23] Giuliano AE, Eilber FR. The rationale for planned reoperation after unplanned total excision of soft-tissue sarcomas. *J Clin Oncol* 1985;3:1344–8.
- [24] Mark W, Manoso , Deborah A, et al. Outcomes of re-excision after unplanned excisions of soft-tissue sarcomas. *J Surg Oncol* 2005;91:153–8.